IN THE SPECIFICATION

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In certain embodiments of the invention, the stem cell is at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% more proliferative than the stem cell incubated without a phosphate mimic under otherwise same conditions.

In certain embodiments, the invention provides a method of identifying a candidate gene that is modulated in a stem cell by treatment with a phosphate mimic, said method comprising the following steps: (a) culturing one or more stem cell populations in the presence of one or more concentrations of the phosphate mimic for a 72- to 96-hour period; (b) culturing one or more stem cell populations without the phosphate mimic to the culture for a 72- to 96-hour period; and (c) identifying any gene that is differentially expressed between the culturing steps (a) and (b) in the stem cell, wherein a gene that is differentially expressed between the culturing steps (a) and (b) is the candidate gene that is modulated in a stem cell by treatment with the phosphate mimic.

In certain embodiments, the invention provides a method as in any of the foregoing paragraphs, wherein the stem cell is a fetal neural stem cell, an adult neural stem cell, an embryonal stem cell or an ependymal neural CNS stem cells.

In certain embodiments, the invention provides a method comprises incubating the neural stem cell in tissue culture medium comprising a phosphate mimic, wherein the incubating step increases formation of neurospheres from the neural stem cell by at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% compared to the formation of neurospheres from the stem cell incubated without phosphate mimic under otherwise same conditions. In one aspect, the neural stem cell is a fetal neural stem cell or an adult neural stem cell.

In certain embodiments, the invention provides a cultured stem cell, wherein the cultured stem cell has been generated by as in any method described in any of the foregoing paragraphs. In certain embodiments, the invention provides a cultured neural stem cell, wherein the cultured neural stem cell has been generated by as in any method described in any of the foregoing paragraphs.

The invention provides a method for culturing a progenitor cell, said method comprising incubating the progenitor cell in tissue culture medium comprising a phosphate

mimic, wherein the incubating step increases intracellular ATP levels in the progenitor cell by at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% compared to intracellular ATP levels in the progenitor cell incubated without phosphate mimic under otherwise same conditions.

The invention further provides a method for culturing a progenitor cell, said method comprising incubating the neural progenitor cell in tissue culture medium comprising a phosphate mimic, wherein the progenitor cell is at least 25% more proliferative than the neural progenitor cell incubated without a phosphate mimic under otherwise same conditions, and wherein the proliferation is measured by a method comprising: (a) culturing one or more progenitor cell populations in the presence of one or more concentrations of the phosphate mimic for a 72- to 96-hour period; (b) culturing one or more progenitor cell populations without the phosphate mimic to the culture for a 72- to 96-hour period; and (c) determining the number of viable progenitor cells at the end of the 72- to 96-hour period in the stem cell populations of step (a) and (b), respectively, and wherein the culturing steps (a) and (b) are conducted under otherwise the same conditions. In certain aspects, the neural progenitor cell is at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% more proliferative than the progenitor cell incubated without a phosphate mimic under otherwise same conditions. In certain aspects, the progenitor cell is a neural progenitor cell.

The invention also provides a method for culturing a neural progenitor cell, said method comprising incubating the neural progenitor cell in tissue culture medium comprising a phosphate mimic, wherein the incubating step increases formation of neurospheres from the neural progenitor cell by at least 25% compared to the formation of neurospheres from the neural progenitor cell incubated without phosphate mimic under otherwise same conditions. In certain aspects, the incubating step increases formation of neurospheres from the neural progenitor cell by at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% compared to the formation of neurospheres from the neural progenitor cell incubated without phosphate mimic under otherwise same conditions.

The invention further provides a methods as described in any of the foregoing paragraphs, wherein the culture medium further comprises an agent selected from the group consisting of a GPCR agonist, a GPCR antagonist, an agonist of adenylate cyclase, an antagonist of phosphodiesterase, an antagonist of neurotransmitter uptake, a MAO inhibitor, a COMT inhibitor, a neuropeptide peptidase inhibitor, a Li-salt, an inhibitor of the sarcoplamic-reticulum Calcium-ATPase, an agonist of IP3, an agonist of IP3 receptor, a

Calcium ionophore, a cell membrane depolarizing agent, an agonist of guanylate cyclase, an inhibitor of phosphodiesterase, a natriuretic peptide and a natriuretic peptide mimics.

In certain embodiments, the invention provides a culture medium for culturing stem cells, wherein the culture medium comprises a phosphate mimic, wherein the culture medium has not been supplemented with any exogenously added growth factor, and wherein the culture medium supports the proliferation of the stem cell.

In certain embodiments, the invention further provides a culture medium for culturing stem cells, wherein the culture medium comprises a phosphate mimic, wherein the culture medium comprises one or more growth factors in an amount that is not sufficient to support proliferation of the stem cell in the absence of a phosphate mimic, and wherein the culture medium supports the proliferation of the stem cell.

In certain embodiments, the invention further provides method for culturing a plurality of stem cells, said method comprising incubating the stem cells in tissue culture medium comprising a phosphate mimic, wherein the incubating step elevates the ATP level in the culture by at least 25%, at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% compared to the ATP level in the culture without phosphate mimic under otherwise same conditions.

In certain embodiments, the invention further provides method for culturing a plurality of stem cells, said method comprising incubating the stem cells in tissue culture medium comprising a phosphate mimic, wherein the incubating step elevates the total ATP level of the plurality of stem cells per unit of volume of culture by at least 25%, at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% compared to the total ATP level of the plurality of progenitor cells per the unit of volume of culture without phosphate mimic under otherwise same conditions.

In certain embodiments, the invention further provides method for culturing a plurality of progenitor cells, said method comprising incubating the progenitor cells in tissue culture medium comprising a phosphate mimic, wherein the incubating step elevates the ATP level in the culture by at least 25%, at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% compared to the ATP level in the culture without phosphate mimic under otherwise same conditions.

In certain embodiments, the invention further provides method for culturing a plurality of progenitor cells, said method comprising incubating the progenitor cells in tissue

culture medium comprising a phosphate mimic, wherein the incubating step elevates the total ATP level of the plurality of progenitor cells per unit of volume of culture by at least 25%, at least 50%, at least 100%, at least 200%, at least 300%, at least 400% or at least 500% compared to the total ATP level of the plurality of progenitor cells per the unit of volume of culture without phosphate mimic under otherwise same conditions.